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SHEAR-SENSITIVE INJECTABLE DELIVERY SYSTEM

Technical Field

The invention relates to a system for use in the delivery of a material into the body of a mammal and a method of using such a system. More particularly, the invention relates to a system for use in delivering a shear-sensitive injectable material into the body of a mammal to bulk-up, augment, or replace tissue.

Background Information

Shear-sensitive injectable materials have a variety of medical applications. These materials may be used as bulking agents to strengthen tissues weakened by old age and/or disease, as implants to contour overlying tissue (e.g., in plastic surgery applications), or as prosthetic implants, acting as replacement tissue. In some instances, it is desirable to use a shear-sensitive injectable material as an embolic, for example, in the occlusion of abnormal blood vessels. Typical shear-sensitive injectable materials comprise a cross-linked polysaccharide or hydrogel, a carrier (typically a hydrophobic material such as oil), and matrix materials, providing paste-like compounds useful to bulk up tissue.

Current methods and delivery systems for delivering shear-sensitive injectable materials to a tissue, or to a space adjacent to a tissue, have certain disadvantages. A typical delivery system used is a syringe comprising a tube and a plunger. During the injection process, the carrier/hydrophobic material has a tendency to separate from the matrix material within the tube of the syringe, resulting in carrier-only injection into a tissue. Separation may be caused by a number of factors including shelf-life, material separation, excessive pressure in the syringe applied by the plunger, pushing the carrier/hydrophobic material ahead of the matrix material, or the use of an injection needle having a diameter which is too small. When a carrier is not well mixed, the matrix material is difficult to advance through the syringe with the plunger. Ultimately, the physician is unable to gauge properly the amount of bulking material he or she is actually injecting, resulting in the necessity for multiple treatments and discomfort to the patient.

Summary of the Invention

It is an object of the present invention to provide a system for delivering a shear-sensitive injectable material. As defined herein, a "shear-sensitive injectable material" is a material which comprises components, or is itself a component, which is subject to shear (e.g., causing degradation or a change in viscosity) upon mixing and passage through a standard-sized needle (e.g., about 10 gauge to about 25 gauge). In the process of mixing, shear-sensitive injectable materials form paste-like compounds which are ideal for implantation into the body because they conserve their volume and do not migrate far from a site of injection. Such materials are useful in applications to bulk-up, augment, or replace tissues.

The present invention relates to a delivery system for delivering a shear-sensitive injectable material into the body of a mammal, such as a human being. The delivery system acts as a mechanical feed which continuously mixes a shear-sensitive injectable material as it delivers the shear-sensitive injectable material to a target tissue, or to a site adjacent a target tissue, within the body of a mammal. In one embodiment of the invention, the delivery system is composed of an injector system having a rotatable mixing member coupled to a driving system.

The injector system comprises an injector housing defining a lumen and having an output end coupled to a needle assembly for coupling to a needle and a driving system connection end for coupling to a drive mechanism. A mixing member extends within the lumen of the injector housing from the driving system connection end of the housing to at least the output end, and is rotatable within the lumen to feed the shear-sensitive injectable material out through the output end through the needle assembly. In a further embodiment of the invention, the injector housing comprises a feeder and a reservoir; the reservoir coupled at one end to the feeder and at the other end to a needle assembly. In this embodiment, the mixing member rotates within the feeder to feed a shear sensitive injectable material into the reservoir and moves linearly within the reservoir portion to push the shear-sensitive injectable material through the needle assembly.

A driving system is provided for use with the injector system. The driving system includes a drive mechanism in communication with an actuator which is capable of actuating the

drive mechanism. An interfacing member is coupled to the drive mechanism and is for coupling to the mixing member of the injector system. In operation, the driving system is coupled to the injector system via the interfacing member. Actuation of the drive mechanism causes the mixing member to rotate within the lumen of the injector housing, thereby to mix and deliver a shear-sensitive injectable material within the injector housing through the output end of the injector housing to an injection site. In one embodiment of the invention the actuator comprises a switch and is coupled to an energy source, such as a battery, which is in electrical communication with the drive mechanism.

In another embodiment of the invention, the injector system is loaded with a shear-sensitive injectable material and is provided within a packaging to maintain the sterility of the injector system. In this embodiment, the injector system is ready to be coupled to the drive mechanism of the driving system and to be injected into the body of a mammal.

In yet another embodiment of the invention, a coupling system is provided for coupling to a tube of a syringe. The coupling system adapts the tube of the syringe to deliver a shear-sensitive injectable material into the body of a mammal. The coupling system has a coupling housing capable of mating with the tube of the syringe. A drive mechanism is positioned within the coupling housing and is capable of providing a rotary force upon actuation by the user. The coupling system also includes a mixing member which is for coupling to the drive mechanism and which extends within the tube of the syringe when the coupling housing is mated to the tube of the syringe. Upon actuation of the drive mechanism, the mixing member rotates in response to rotary force from the drive mechanism. The rotation of the mixing member simultaneously mixes and delivers a shear-sensitive injectable material loaded within the syringe. In some embodiments of the invention, the coupling housing further comprises an actuator for actuating the drive mechanism. In yet other embodiments of the invention, the coupling housing comprises finger grips for ease of manipulation of the housing and tube of the syringe during the injection process.

Brief Description of the Drawings

In the drawings, like reference characters generally refer to the same parts throughout the different views. Also, the drawings are not necessarily to scale, emphasis instead generally being placed upon illustrating the principles of the invention.

Figure 1 shows one embodiment of a delivery system according to the invention wherein the drive system features finger grips for ease of manipulation.

Figure 2 is a schematic longitudinal view of one embodiment of an injector system according to the invention.

Figures 3A-3E show views of mixing members according to the invention. Figure 3A shows a mixing member having variably spaced threads and a constant outer diameter. Figure 3B shows a mixing member having uniformly spaced threads and a varying outer diameter. Figure 3C shows a mixing member having both variably spaced threads and a varying outer diameter. Figure 3D shows a mixing member having a constant outer diameter and multiple starts. Figure 3E shows a mixing member having threads with a varying radial height and a constant outer diameter.

Figure 4 shows one embodiment of a drive system according to the invention.

Figure 5 shows one embodiment of a coupling system according to the invention.

Figures 6A-B show an embodiment of a delivery system which is capable of operating in both a feed mode and a plunger mode. Figure 6A shows the device operating in a feed mode. Figure 6B shows the device operating in a plunger mode.

Description

Referring to Figure 1, the delivery system **1** may be used for delivering a shear-sensitive injectable material **13** into the body of a mammal. The delivery system **1** acts as a mechanical feed to mix continuously a shear-sensitive injectable material **13** as it is delivered to a tissue or to

a site adjacent to a tissue within the body of a mammal. The delivery system **1** comprises an injector system **9** (shown alone in Figure 2) and a driving system **19** (shown alone in Figure 4).

In one embodiment of the invention, and referring to Figure 2, the injector system **9** comprises an injector housing **7** defining a lumen **7L** and having an output end **16** and a driving system connection end **17**. A mixing member **10** extends within the lumen **7L** of the injector housing **7** from the driving system connection end **17** to at least the output end **16**. The mixing member **10** rotates within the lumen **7L** to mix and deliver an injectable **13** into the body of a mammal. Rotation of the mixing member causes a shear-sensitive injectable material within the lumen **7L** to move forward to the output end **16** causing ejection of the shear-sensitive material through the output end **16**. The output end **16** has a smaller inner diameter than the lumen **7L** of the of the injector system **9**.

In one embodiment of the invention, the mixing member **10** is in the form of an elongated helical element. Helical elements encompassed within the scope of the present invention include, but are not limited to, augers, screws, corkscrews, and impellers. In one embodiment, shown in Figures 3A-3C, the helical element is a screw **10s** with a substantially conical shape which tapers in the direction of transport of the shear-sensitive injectable material **13**. In a further embodiment of the invention, the screw **10s** comprises threads **10t**. The design of the threads **10t** can be optimized to reduce erosion on the surface of the thread **10t** resulting from contact with the matrix materials within the shear-sensitive injectable material **13** (e.g., by providing rounded, polished ridges).

The outer diameter (**OD**) of the screw **10s** and pitch of its threads **10t** can take multiple forms depending on the delivery requirements (e.g., shear-sensitive injectabe material **13** with more matrix material requires more pressure to deliver). A helical element with a larger **OD** will allow increased pressure to be exerted on the shear-sensitive injectable material **13**; however, this is counterbalanced by increased back-pressure from the shear sensitive injectable material **13**, especially at the output end **16** of the injector system **9**. In one embodiment of the invention (not shown) the **OD** of the screw **10s** approaches the diameter of the lumen **7L**. In another embodiment, shown in Figure 3B, a screw **10s** is provided having an **OD** which gradually decreases from the driving system connection end **17** to the output end **16** of the device, having an **OD** which is just slightly smaller than the diameter of the lumen **7L** proximal to the driving

system connection end **17**. This design prevents excessive pressure on the shear-sensitive injectable material **13** at the output end **16**. A similar effect may be achieved by continuously increasing the pitch of the screw **10s** from the driving system connection end **17** to the output end **16** (as shown in Figure 3B). In another embodiment of the invention, shown in Figure 3C, both the **OD** and pitch of the screw **10s** are varied at the same time.

The threads **10t** of the screw **10s** provide channels through which the shear-sensitive injectable material **13** can flow and enhances mixing of the shear-sensitive injectable material **13** as the screw **10s** rotates. The design and number of starts of the threads **10t** can be varied to maximize mixing. In one embodiment, the radial height **h** of the threads **10t** (i.e., from the base of the thread to its peak) is designed to be smallest at the driving system connection end **17** and greatest at the output end **16** to accommodate a higher proportion of unmixed matrix materials at the driving system connection end **17**. The number of starts of the helical element may also be varied. In one embodiment of the invention, the threads **10t** of the helical element comprise a single start (as in Figures 3A-3C, and 3E). In another embodiment of the invention, as shown in Figure 3D, the threads **10t** of helical element comprise multiple starts.

The mixing member **10** is positioned within the lumen **7L** of the injector housing **7** by a driver guide **11**. The driver guide **11** is located proximal to the driving system connection end **17** of the injector housing **7** and is held in place by a rubber stopper **6** when the injector **9** is not in use (i.e., when the mixing member **10** is not rotating). The driver guide **11** permits rotational motion of the mixing member **10**, but constrains lateral motion. When the injector system **9** is in operation, the stopper **6** and driver guide **11** move downward (i.e., in the direction of the output end **16**) in the direction of flow of the shear-sensitive injectable material **13**. The rotational motion of the mixing member **10**, and the downward movement of the stopper **6** and driver guide **11**, displaces the shear-sensitive injectable material **13** within the lumen **7L** and ejects it out the output end **16**. The rubber stopper **6** also maintains a seal between the driver guide **11** and the inner wall of the injector housing **7**, preventing leakage of the shear-sensitive injectable material **13** at the driving system connection end **17**. In a further embodiment, of the invention, the injector housing **7** is marked by indices (e.g., lines or tick marks indicating units of measurement such as "cc", "ml", or "oz.") allowing the user to monitor the amount of shear-sensitive injectable material **13** being delivered.

The injector system **9** further comprises a needle assembly **18** which may be an integral part of the injector housing 7, or which may be insert-molded onto an end **7d** of the injector housing 7 distal to the motor connection end **17**. The needle assembly **18** further comprises a needle **8** which may be an integral part of the needle assembly **18** or may be fitted onto the end **18e** of the needle assembly **18** (e.g., by screwing onto threads fabricated at the end **18e** of the needle assembly **18** or by luer lock). In this embodiment of the invention, standard needles **8** used in the art may be coupled to the end **18e** of the needle assembly **18**. In one embodiment of the invention, the distal end of the needle **8** is reduced in diameter to allow for a constant cross-sectional area through which to deliver or feed shear-sensitive injectable material **13**. The diameter of the needle **8** should be small enough to permit injection into, or adjacent to, a target site within the body (e.g., about 10 gauge to about 25 gauge).

Shear-sensitive injectable material **13** can be used to bulk-up, augment, or replace a tissue. In one embodiment, the shear-sensitive injectable material **13** is a paste-like compound comprising a crosslinked material, a carrier, and a matrix material. Suitable crosslinked materials include, but are not limited to, collagen, polymers or copolymers of acrylonitrile, vinyl acetate, methacrylate, alginates, hydrogels, polyvinylpyrrolidone, hyaluronic acid, fibrin, polygalacturonic acid, propylene glycol alginic acid, polyarabinic acids, gum cappacarrageen, polyphosphazenes, block copolymers such as polyethylene oxide-polypropylene glycol blocks, and combinations thereof. Crosslinking may be performed by exposing a crosslinkable material to changes in temperature, pH, or radiation. Chemical agents (non-ionic and ionic crosslinking agents) may also be used.

Suitable carrier materials are generally hydrophobic, and include, but are not limited to, oil, liquid polymers, liquid surfactants, and liquid plasticizers. Suitable matrix materials include, but are not limited to, fiber, chopped suture material, textured yarn material, ground suture material, ground fabric, polyester material, polytetrafluoride beads, silicon particles, polytetrafluoroethylene (PTFE) particles, ceramic particles, carbide particles, and combinations thereof. In embodiments where particles are used, particle diameters range from about 50 to about 250 microns. Ideal shear-sensitive injectable materials **13** are injectable, do not migrate a substantial distance from the injection site, and conserve their volume.

In another embodiment of the invention, bioactive materials may be additionally included with the shear-sensitive injectable material **13**, such as proteins (e.g., growth factors, antibodies, ligands, receptors), naked or encapsulated nucleic acids (e.g., DNA, RNA, PNA molecules, aptamers, antisense molecules, and ribozymes), drugs, therapeutic agents, and the like. In a further embodiment of the invention, the shear-sensitive injectable material **13** is a material which may be injected into the body of mammal (e.g., a rabbit) to stimulate an immune response, i.e., such as polyacrylamide. In certain embodiments of the invention, the shear-sensitive injectable material **13** further comprises proteins, protein fragments, polypeptides (natural or synthetic), antigens, and the like.

In one embodiment of the invention, the injector system **9** is loaded with the shear-sensitive injectable material **13** and is provided within a packaging to maintain the sterility of the injector system **9**. In this embodiment, the injector system **9** is ready to be coupled to the driving system **19** and the shear-sensitive injectable material **13** is ready to be injected into the body of a mammal. In general, the housing **7** of the injector system **9**, including the needle assembly **18**, with, or without the needle **8**, is made of a material that is able to withstand conditions needed to sterilize or decontaminate it (e.g., autoclaving, irradiation, and/or exposure to chemical agents and/or anti-microbial agents) and is biocompatible. Suitable housing **7** materials include polypropylene, plastic, Teflon® material, PVC, and the like.

In a one embodiment of the invention, shown in Figure 4, a driving system **19** is provided for use in connection with the injector system **9**. The driving system **19** comprises a drive mechanism **3** in communication with an actuator **15** which is capable of actuating the drive mechanism **3**. An interfacing member **12** is coupled to the drive mechanism **3** and is for coupling to the mixing member **10** of the injector system **9**.

In operation, as shown in Figure 1, the drive mechanism **3** is coupled to the injector system **9** via the interfacing member **12**. In this embodiment of the invention, the delivery system **1** acts entirely in a "feed mode." Actuation of the drive mechanism **3** by the actuator **15** causes the mixing member **10** to rotate within the lumen **7L** of the injector housing **7**, thereby to mix and feed the shear-sensitive injectable material **13** disposed within the injector housing **7** through the output end **16** to an injection site (e.g., via the needle assembly).

In another embodiment of the invention, and referring to Figures 1, 4, and 5, the drive mechanism **3** is a motor which is contained within a motor housing **13** and includes a shaft **23** which is adapted for coupling to the interfacing member **12**. In this embodiment of the invention, mechanical rotary force from the shaft **23** is transmitted through the interfacing member **12** to the mixing member **10**, thereby rotating the mixing member **10** within the lumen **7L** of the injector **9**.

In one embodiment of the invention, shown in Figure 4, the drive mechanism **3** comprises an electric motor **20** which includes a conducting loop **22** mounted on a shaft **23** made of insulating material. A magnetic field around the loop **22**, supplied by a magnet **21**, causes the loop **22** to rotate when a current flows through it. The loop **22** causes the shaft **23** to rotate, transmitting rotary force to the mixing member **10** via the interfacing member **12**. In another embodiment of the invention, the electric motor **20** is a DC motor and further comprises a commutator (not shown) for switching the direction of an electric current to maintain the shaft **23**'s direction of motion. In another embodiment of the invention, the drive mechanism **3** comprises a stationary loop **22** and a movable magnet **21**. In a further embodiment of the invention, the motor **20** is a high torque low speed DC motor controlled by a switch.

The drive mechanism **3** may further include electrical connection elements **24** for connecting the motor **20** to an energy source **2**, such as a battery. In one embodiment of the invention, shown in Figure 4, the flow of energy (e.g., current) from the energy source **2** is controlled by an actuator **15** to which it is coupled by electrical elements **15c**. In a further embodiment of the invention, the actuator **15** comprises a switch which can be turned on and off by an operator.

In another embodiment of the invention, shown in Figures 6A-B, the delivery system **1** may be operated in both a feed mode and a "plunger mode." In this embodiment, the housing of the injector system defines a feeder **7f** and a reservoir **7r.** The reservoir **7r** has a proximal end **27p** and a distal end **27d.** The proximal end **27p** of the reservoir **7r** is coupled to the end of feeder **7f** distal from the driving system connection end **17** while the distal end **27d** of the reservoir is coupled to the needle assembly **18.** In one embodiment of the invention, the feeder **7f** and reservoir **7p** comprise a single unit molded together, while in another embodiment of the invention, the reservoir **7r** is a module which can be separated from the feeder **7f.**

During the feed mode of operation, shown in Figure 6A, the tip **10tp** of the mixing member **10** terminates within the feed portion **7f** of the delivery system **1**. Rotation of the mixing member **10** within the feed portion **7f** by the drive mechanism **3** then feeds the shear-sensitive injectable material **13** into the reservoir portion **7r** of the delivery system **1**. During the plunger mode of operation, shown in Figure 6B, a linear force is exerted on the mixing member **10**, either manually, mechanically, or through the use of the drive mechanism **3**, and the mixing member **10** is used as a plunger to push shear-sensitive injectable material **13** within the reservoir **7r** through the needle assembly **18**. This embodiment of the invention allows more force to be developed at the needle assembly **18** portion of the device, making it easier to inject the shear-sensitive injectable material **13** into a target tissue.

In a further embodiment of the invention, shown in Figure 5, a coupling system **25** is provided for coupling to a tube of a syringe. The coupling system **25** is for adapting the tube of the syringe to deliver a shear-sensitive injectable material **13** into the body of a mammal. The coupling system **25** comprises a coupling housing **26** capable of mating with the tube of the syringe at mating portion **4** of the coupling housing **26** (e.g., by a twisting and locking motion). A drive mechanism **3** is positioned within the coupling housing **26** and is capable of providing a rotary force upon actuation. The coupling system **25** also includes mixing member **10** which is for coupling to the drive mechanism **3** via interfacing member **12** and which extends within the tube of the syringe when the coupling housing **26** is mated to the tube of the syringe.

Upon actuation of the drive mechanism **3**, the mixing member **10** rotates in response to force from the drive mechanism **3**. The rotation of the mixing member **10** within the lumen **7L** simultaneously mixes and delivers a shear-sensitive injectable material **13** loaded within the tube of the syringe. In another embodiment of the invention, the coupling housing **26** further comprises an actuator **15** for actuating the drive mechanism **3**.

It should be apparent to those of skill in the art that the exact configuration of the housing **26** may be modified in many ways without affecting the operation of the coupling system **25**. In one embodiment of the invention, the coupling housing **26** comprises finger grips **5** for ease of manipulation of the coupling system **25** and syringe during the injection procedure, and can be manipulated with one or both hands. In another embodiment of the invention, a high torque low speed DC torque motor **20** is provided within the coupling housing **26**. The motor **20** is

actuatable by a switch that an operator can easily manipulate with a thumb while gripping the outside of the coupling housing **26**. The intent is to provide an ergonomic feel to the user so that he or she may have or perceive control of the flow rate of material **13** exiting the syringe.

Although the mixing member **10** is shown coupled to the interfacing member **12** in Figures 5, 6A and 6B, the various components of the coupling system **25** may be provided separately, i.e., in the form of a kit, which may optionally include the tube of a syringe. The tube of the syringe may further be provided in a sterile or sterilizable packaging. In another embodiment of the invention, the mixing member **10** may be provided as part of the injector system **9**, and may additionally include the shear-sensitive injectable material **13**. Any of the injector system **9**, or injector system **9** with shear-sensitive injectable material **13**, may also be provided within a sterile or sterilizable packaging.

The coupling system **25** of the present invention may be adapted for coupling to a variety of standard sized syringes known in the art, from 1 cc to 50 cc. In one embodiment of the invention, the coupling system **25** is adapted for coupling to the injector system **9** discussed above, which may also be molded to a variety of sizes, and which may include indicia against which to measure the amount of shear-sensitive injectable material **13** being delivered (e.g., markings indicating "ml," "cc," or "oz." When injecting a shear-sensitive injectable material **13** to bulk-up, augment or replace tissue, a syringe or injector system **9** is selected which is capable of delivering an amount of shear-sensitive injectable material **13** suitable for a desired medical procedure. For example, the amount of material used for augmentation of anal sphincters is generally from 14-40 cc, and typically from about 20-30 cc, while the amount of shear-sensitive injectable material **13** that is used for muscle repair is typically from about 5 to about 10 cc.

Although the delivery system **1** of the present invention is particularly suited for the delivery of a shear-sensitive injectable material **13**, because of its ability to act as a mechanical feed, it should be readily apparent to those of skill in the art, that the system may be used to deliver a variety of injectable materials, including fluids, to a target site.

Having thus described certain embodiments of the present invention, various alterations, modifications, and improvements will be apparent to those skilled in the art. Such variations, modifications, and improvements are intended to be within the spirit and scope of the invention.

The materials employed, as well as their shapes and dimensions, generally can vary. Accordingly, the foregoing description is by way of example only and is not intended to be limiting.

What is claimed is: